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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/919,196	07/31/2001	Ming-Fong Lin	UNMC.63157	3974

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DANN DORFMAN HERRELL & SKILLMAN  
SUITE 720  
1601 MARKET STREET  
PHILADELPHIA, PA 19103-2307

EXAMINER

DAVIS, MINH TAM B

ART UNIT	PAPER NUMBER
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1642

DATE MAILED: 01/27/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

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**Office Action Summary**

Application No.

09/919,196

Applicant(s)

LIN, MING-FONG

Examiner

MINH-TAM DAVIS

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 05 November 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-11 is/are pending in the application.
- 4a) Of the above claim(s) 5-11 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-4 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 4.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

### DETAILED ACTION

Applicant's election with traverse of group I, claims 1-4, species cell line NE-1-3 in Paper No. 6 is acknowledged. The traversal is on the ground(s) that 1) USC 121 states that if two or more independent and distinct inventions are claimed in one application, the Director may require the application to be restricted to one of the invention, 2) The restriction is improper, because the subject matters of group I and II-VI are related, and as agreed by the Examiner that they are related as product and process, they are not independent inventions, 3) It has been a practice to examine a cell line and a method for producing the same or a method for using the same in one application, as shown in some issued patents, 4) Groups III and V have the same classification, and similarly groups IV and VI have the same classification, and thus there is no indication that the field of search would be different in these invention, and 5) it is improper to require species election of different cell lines because they share similar properties, i.e. similar expression patterns of NE-specific biomarkers. This is not found persuasive because of the following reasons: 1) Although the Director "may" require the application containing if two or more independent and distinct inventions to be restricted to one of the invention, there is no requirement by the Director to examine all the groups for this instant application, 2) It is proper according to 35 USC 121 to restrict different distinct and independent inventions that are related to each other as product and process, 3) Although in some issued patents, a cell line has been examined together with a method for producing the same or a method for using the same in one application, different applications are considered separately and independently of each

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other, 4) Although Groups III and V have the same classification, and similarly Groups IV and VI have the same classification, the searches for these groups are not-coextensive, because the searches are complex and require different database, and are not based solely in classification search.

The requirement is still deemed proper and is therefore made FINAL.

It is noted that the species biomarkers are not applied to the present claims 1-4, since they are not drawn to a cell line having specific markers. However, if the claims are amended to a cell line having specific markers, election of a species biomarker would be required.

After review and reconsideration, different species cell lines however are rejoined.

Accordingly, claims 1-4, NE-1-3, NE-1-8, and NE-1-9 cell lines are examined in the instant application.

#### DEPOSIT REQUIREMENT

*cancel cl 4 - withdrawn*  
1. The specification is objected to and claim 4 is rejected under 35 U.S.C. § 112, first paragraph, as failing to provide an adequate written description of the invention and failing to provide an enabling disclosure, because the specification does not provide evidence that the claimed biological materials are (1) known and readily available to the public; (2) reproducible from a written description (e.g. sequenced); or (3) deposited.

The claim 4 is drawn to cell line NE-1-9. There is however no deposit information concerning the cell line NE-1-9 in the specification.

*not deposited, only NE-1-3  
NE-1-8*

It is unclear if a cell line which has the exact characteristics and chemical identity of NE-1-9 is known and publicly available, or can be reproducibly isolated without undue experimentation. Clearly, without access to the cell line NE-1-9, it would not be possible to practice the claimed invention. Therefore, a suitable deposit for patent purposes is suggested. Without a publicly available deposit of the above cell line, one of ordinary skill in the art could not be assured of the ability to practice the invention as claimed. Exact replication of: (1) the claimed cell line is an unpredictable event.

If a deposit has been made under the provisions of the Budapest Treaty, filing of an affidavit or declaration by applicant or assignees or a statement by an attorney of record who has authority and control over the conditions of deposit over his or her signature and registration number stating that the deposit has been accepted by an International Depository Authority under the provisions of the Budapest Treaty, that all restrictions upon public access to the deposits will be irrevocably removed upon the grant of a patent on this application and that the deposit will be replaced if viable samples cannot be dispensed by the depository is required. This requirement is necessary when deposits are made under the provisions of the Budapest Treaty as the Treaty leaves this specific matter to the discretion of each State.

In addition to the conditions under the Budapest Treaty, applicant is required to satisfy that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent in U.S. patent applications and that the deposit will be replaced if viable samples cannot be

dispensed by the depository is required. Applicant's provision of these assurances would obviate this objection/rejection.

Affidavits and declarations, such as those under 37 C.F.R. § 1.131 and 37 C.F.R. § 1.132, filed during prosecution of the parent application do not automatically become a part of this application. Where it is desired to rely on an earlier filed affidavit, the applicant should make the remarks of record in the later application and include a copy of the original affidavit filed in the parent application

Amendment of the specification to recite the date of deposit and the complete name and address of the depository is required. As an additional means for completing the record, applicant may submit a copy of the contract with the depository for deposit and maintenance of the deposit.

If the original deposit is made after the effective filing date of an application for patent, the applicant should promptly submit a verified statement from a person in a position to corroborate the fact, and should state, that the biological material which is deposited is a biological material specifically identified in the application as filed, except if the person is an attorney or agent registered to practice before the Office, in which the case the statement need not be verified. See MPEP 1.804(b)..

2. Further, although the specification provides the name and accession number of the cell lines NE-1-3 and NE-1-8, the date of the deposition, and the name and address of the depositor, where the cells are deposited (page 10, second paragraph), the specification fails to provide an affidavit or declaration stating that all restrictions upon public access to the deposits will be irrevocably removed upon the granting of a patent

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on this application, and that the deposit will be replaced if viable samples cannot be dispensed by the depository is required.

The identifying information set forth in 37 CFR 1.809(d) should be added to the specification. See 37 CFR 1.803-1.809 for additional explanation of these requirements.

Claims 2-3 are rejected under USC 112, first paragraph, for the reasons set forth in the objection to the specification.

#### **REJECTION UNDER 35 USC 112, SECOND PARAGRAPH**

Claims 2-4 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 2-4 are rejected as being indefinite for the use of designation "NE-1-3, NE-1-8, NE-1-9" as the sole means of identifying the claimed cell lines. The use of laboratory designation only to identify a particular cell line renders the claims indefinite because different laboratories may use the same laboratory designations to define completely distinct cell lines. Amendment of the claims to include physical and/or functional characteristics of "NE-1-3, NE-1-8, NE-1-9" which unambiguously define "NE-1-3, NE-1-8, NE-1-9" is required.

#### **REJECTION UNDER 35 USC 112, FIRST PARAGRAPH, SCOPE**

If Applicant could overcome the above deposit requirement, claims 1-4 are still rejected under 35 U.S.C. 112, first paragraph, because the specification, while being

enabling for a cell line NE-1-3, or NE-1-8, NE-1-9 stored in hormone deficient medium, does not reasonably provide enablement for a cell line NE-1-3, or NE-1-8, NE-1-9 stored in any medium. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 1-4 are drawn to a human prostate cancer-associated neuroendocrine (NE)-like cell line, which is NE-1-3, NE-1-8 or NE-1-9.

Claims 1-4 encompass a human prostate cancer-associated neuroendocrine (NE)-like cell line, which is NE-1-3 which are stored in any type of medium.

The specification discloses that the claimed NE-like cell lines are cloned from LNCaP cells that were exposed to medium with low testosterone, and acquired NE characteristics (p.10-11).

One cannot extrapolate the teaching in the specification to the claims because one would have expected that the claimed cell lines would be unstable and loose the NE characteristics under any type of medium. Cox ME et al, 1999, Cancer Research, 59(15): 3821-30, IDS # C18 in paper No:4 of 03/12/02, teach that LNCaP cells acquire NE characteristics in response to the presence of cyclic AMP, possibly by an increase in intracellular cyclic AMP. Cox et al further teach that the NE phenotype is rapidly lost upon withdrawing of the inducing agents. Burchardt, T et al, 1999, J Urol, 162(5): 1800-5, teach that LNCaP cells in hormone-deficient medium have 9 fold increase in cyclic AMP and transdifferentiate into a neuroendocrine cell phenotype. Thus one would have expected that the LNCaP cells that were exposed to medium with low testosterone, and



acquired NE characteristics as disclosed in the specification would have an increase in cyclic AMP in a hormone-deficient medium, wherein said increase in cyclic AMP is responsible for the cell transdifferentiation into a neuroendocrine cell phenotype.

Further, one could not have predicted that in any type of medium, the inducing level of cyclic AMP in LNCaP would be maintained, and thus it is unpredictable that the claimed cell lines in any type of medium would be stable.

In view of the above, it would have been undue experimentation for one of skill in the art to practice the claimed invention.

#### **REJECTION UNDER 35 USC 102**

Claim 1 is rejected under 35 USC 102(b) as being anticipated by Cox et al, *supra*, or Burchardt et al, *supra*, or Shen et al, 1997, Urol Oncol, 3: 67-75, IDS # C16 in paper No:4 of 03/12/02.

Claim 1 is drawn to a human prostate cancer-associated neuroendocrine (NE)-like cell line.

Cox et al teach LNCaP cells that are induced to acquire NE characteristics by the presence of cyclic AMP in the medium.

Burchardt et al teach LNCaP cells that are transdifferentiated into a neuroendocrine cell phenotype in a hormone-deficient medium.

Shen et al teach LNCaP cells that transdifferentiated into neuroendocrine cell phenotype in a hormone-depleted medium.

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Thus the cell lines taught by Cox et al or Burchardt et al, or Shen et al seem to be the same as the claimed cell lines.

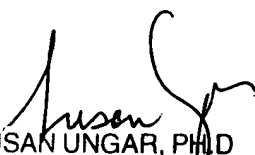
Any inquiry concerning this communication or earlier communications from the examiner should be directed to MINH-TAM DAVIS whose telephone number is 703-305-2008. The examiner can normally be reached on 9:30AM-4:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, ANTHONY CAPUTA can be reached on 703-308-3995. The fax phone numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0916.

MINH TAM DAVIS

January 23, 2003

  
SUSAN UNGAR, PH.D  
PRIMARY EXAMINER